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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,333	11/14/2001	Larry Wayne Oberley	875.042US1	5690

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EXAMINER	
SCHULTZ, JAMES	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,333	OBERLEY ET AL.	
	Examiner	Art Unit	
	J. D. Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-8,11-15 and 18-26* is/are pending in the application.

4a) Of the above claim(s) *5 and 23-26* is/are withdrawn from consideration.

5)☒ Claim(s) *20 and 21* is/are allowed.

6)☒ Claim(s) *2,3,6-8,11-15,18,19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the invention of Group I, claims 2, 3, 6-8, 11-15, and 18-22, directed to antisense compounds and methods of targeting the human antioxidant enzyme manganese superoxide dismutase in the reply filed on 30 May 2006 is acknowledged. The traversal is on the assertion that the inventions are closely related, and because restriction is optional in all cases, and because applicants believe a full search and examination of the instant claims including all recited targets does not constitute a burden. This is not found persuasive because as stated in the restriction requirement, each sequence has both a unique structure and function which is not shared by any other sequence, which therefore requires a unique search and examination, which is considered a burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6, 23-26, and the subject matter of claims 6 and 7 not drawn to the elected human antioxidant enzyme manganese superoxide dismutase are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 30 May 2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18 and 19 recite the limitation "the portion of the nucleic acid for the antioxidant enzyme" in claim 8. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 11-15, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of breast cancer using the claimed antisense oligonucleotides, does not reasonably provide enablement for treatment of any cancer using the claimed antisense oligonucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The above invention is drawn to methods of treating tumors in a mammal comprising reducing antioxidant enzyme levels in a cell by administering an antisense oligo directed to the start codon of a nucleic acid encoding manganese superoxide dismutase, and to such methods whereby the antisense agent is injected into the tumor, or wherein the mammal is a human, or wherein the antisense agent further comprises a delivery vehicle, which may be lipofectamine or DOTAP, or wherein the antisense oligonucleotide contains phosphorothioate modifications.

The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims is rather broadly drawn to methods of treating any tumor comprising administering an antisense oligo of the invention. The nature of the invention relies upon the inhibition of expression of a specific mRNA using nucleic acid therapeutics in the whole animal (i.e. *in vivo*). While the level of one of ordinary skill practicing the instant invention would be high, the level of predictability is considered to be extremely variable as evident in the prior art (discussed in detail below), and is not considered to provide, in and of itself, sufficient enablement to practice the invention as claimed. This is primarily considered true because the amount of direction provided by the inventor is considered to contradict similar results found in the prior art, since the working examples of the invention as instantly claimed appear to run counter to those results of the prior art. The quantity of experimentation needed to make or use the invention based on the content of the disclosure alone is therefore not enabling for practice of the instant invention *in vivo*.

The specification describes prophetic methods of treatment using antisense oligos targeted to human manganese superoxide dismutase, and further exemplifies method of using the claimed composition to inhibit the expression of human manganese superoxide dismutase in a mouse xenograft injected with MCF-7 cells, which had the effect of inhibiting tumor growth in said model.

A review of the prior art demonstrates that the claimed method, which depends on the administration of an antisense oligo directed to human manganese superoxide dismutase, could not work over the entirety of the claimed breadth. While applicants have demonstrated the

inhibition of tumor growth of a xenograft in a mouse model using the claimed antisense oligo, there is evidence in the prior art that suggests that that inhibition of the identical target would have the opposite effect in at least one other cancer type. For example, Church et al. (Procl. Natl. Acad. Sci 1993, 90:3113-3117, applicants IDS) teach that increasing manganese superoxide dismutase expression actually suppresses the malignant phenotype of human melanoma cells. This runs contrary to the underlying principle of the instantly claimed invention, whereby inhibition of the same target is claimed to suppress the malignant phenotype in humans. Accordingly, the claimed invention cannot work over its entire breadth, since the combination of the specification and the prior art teach suppression of malignancy resulting from both increasing and decreasing the expression of the instantly recited target.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 3, 6, 7, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Kinscherf et al. (FASEB J. 1998, 12:461-467).

The claims of the instant invention are drawn to an oligonucleotide comprising an antisense nucleic acid sequence that is about 18 to 26, or about 20, nucleotides in length, is at least 90% or 100% complementary to and capable of specifically binding to a contiguous portion of a nucleic acid that encodes a human manganese superoxide dismutase, wherein the contiguous

portion includes the start codon of the nucleic acid encoding the human antioxidant enzyme, and to such antisense sequences which contain phosphorothioate linkages.

Kinscherf et al. teach an antisense nucleic acid sequence containing phosphorothioate linkages that is 22 nucleotides in length, which is considered to be about 20, and is 100% complementary to the start codon of the nucleic acid encoding the human manganese superoxide dismutase.

Allowable Subject Matter

Claims 20 and 21 are allowed, because they are free of the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. D. Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JDS

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER